Spheres of Influence

Ethical, Legal, and Social Issues of the Human Genome Project: What to Do with What We Know

Since fisal year 1991, the U.S. Human Genome Project has spent $170.6 million in federal funds to help isolate genes associated with Huntington's disease, amyotrophic lateral sclerosis, neurofibromatosis types 1 and 2, myotonic dystrophy, and fragile X syndrome and to localize genes that predispose people to breast cancer, colon cancer, hypertension, diabetes, and Alzheimer's disease. Now comes the hard part.

Biology's 21st century megaproject starts to look relatively manageable compared to another challenge facing the enterprise: sorting out ethical, legal, and social issues associated with using this information. "The Human Genome Project," wrote Senior Editor Barbara Jasny in the October 1 *Science* editorial, stretches "the limits of the technology and the limits of our ability to ethically and rationally apply genetic information to our lives."

Priorities

Concerned about potential misuse of detailed genetic information, NIH in 1992 created the Ethical, Legal and Social Implications (ELSI) Branch of the project, which receives 3% of the multimillion-dollar genome budget. In the 1993 progress report, Michael Gottesman, acting director of NIH Intramural Research, introduces the most urgent research, educational, and policy issues, including developing consent and confidentiality guidelines for research with human subjects; determining a professional standard of care for delivering new genetic services; developing uniform standards governing the privacy of organs, blood, and tissues banked for clinical purposes; protecting against employment and insurance discrimination based on genetic information; and improving public understanding of the potential and limits of genetics to prevent overly deterministic readings of genetic test results that expose people to social stigma.

Researchers also will study the eugenics movement and other social uses and misuses of genetic research, the likely priority of new genetic services in the health care system, the effects of commercialization on genetic services and research, and sociological implications of the genome project's dynamics and priorities.

Lurking between the lines in this priority list are all the elements that constitute what surely will be an extended debate, not only about whether and how to use life's ultimate database but, as David Heyd writes in *Genethics: Moral Issues in the Creation of People*, about "tampering with the natural biological process of species evolution and individual evolution . . . a form of metaphysical trespass."

ELSI

According to the *1991–1992 Progress Report of the National Center for Human Genome Research*, ELSI aims to develop programs addressed at understanding the project's ethical, legal, and social implications and to define major issues and develop policy to address them. Knowledge gained through the genome project can be used by scientists in many ways: to unravel the pathogenesis of a disorder or understand the expression of a normal human trait, to develop clinical tests for disease or trait-specific forms of the gene, and to detect chemical-specific patterns of genetic changes.

But the effects of getting and using this knowledge create tough choices for nearly everyone. The progress report elaborates:

- Individuals and families must decide whether to participate in testing, with whom to share the results, and how to act on them.
- Health professionals must decide when to offer testing, how to ensure its quality, how to interpret the results, and to whom they disclose information.
- Employers, insurers, the courts, and other social institutions must decide the relative value of genetic information in the decisions they make.
- Governments must decide how to regulate production and use of genetic tests and the resulting information and how to make testing and counseling services accessible.
- Society must decide how to improve public understanding of science and its social implications and increase public participation in science policy making.

Concerns

The presymptomatic DNA-based diagnosis would seemingly eliminate much pain and suffering. It also, according to Jasny's *Science* editorial, "poses a challenge to a society that has not demonstrated a clear ability to evaluate risks and make reasoned choices."

Knowledge about whether someone has a genetic tendency toward a disease could invite social prejudices, a 1988 National Academy of Sciences report said. Health insurance companies could use genetic information to reject people who might be inherently risky investments, for example, or employers could reject prospective employees for similar reasons. In November, a committee of the Institute of Medicine of the National Academy of Sciences released a report outlining policy guidelines and legislative recommendations designed to "avoid involuntary and ineffective testing and to protect confidentiality." The report, *Assessing Genetic Risks: Implications for Health and Social Policy*, identifies concerns such as quality control measures, including federal oversight for testing laboratories, and better genetics training for medical practitioners. It also recommends such measures as voluntary screening and genetic counseling for couples in high-risk populations and urges caution in using and interpreting presymptomatic or predictive tests. Also needed, according to the report, are increased public education about genetics and a national advisory committee to set genetic testing standards.

Thomas Murray summarizes these and other ethical concerns in "Ethical Issues in Human Genome Research," from *The Ethical Dimensions of the Biological Sciences.* "The most important movement in the ethics of workplace genetic testing," Murray writes, "has been away from the original vision of a public health measure to screening as a way of reducing illness-related costs with no effect on the overall incidence of disease."

Employee illness in the United States costs employers money. Growing health insurance costs are prompting employers to look for ways to reduce costs like health insurance, disability insurance, lost productivity, and training of replacement workers for skilled positions. Increased employer concerns about the costs of illness and the prospect of genetic tests that reveal predispositions to disease, Murray adds, "are fertile ground for the use of such tests to screen workers."

Other factors may prompt insurers to use genetic tests. Once the tests become available, people can be tested privately to learn about their risks for disease. Those who are at risk are likely to buy insurance and in larger amounts. Competition among insurance companies will drive companies to genetic screening. A company that uses

such tests would be able to give lower rates to those with no genetic predisposition to disease and higher rates to those at risk. People offered lower rates are more likely to buy insurance from that company, and those at risk will seek insurance from companies that do no genetic testing. These companies will either raise their rates to avoid bankruptcy or begin using genetic tests.

These are a few of the social and legal questions raised by the availability of genetic testing. But there are medical/ethical questions as well: Is there is a need for a genome program? Are both somatic and germline therapy (somatic therapy corrects defects by adding new genes to cells but does not pass genetic changes to offspring; germline therapy passes genetic changes to future generations) medically and ethically acceptable for therapeutic but not nontherapeutic purposes? Is prenatal diagnosis ethically acceptable except where parents use it strictly for gender identification?

Limits to Benefits

While researchers work to have a complete human sequence by 2005, Kenneth Olden, director of the NIEHS, notes that human disease depends on more than genetics. "We've spent a lot of effort and financial resources to understand the role of genetics in human disease and dysfunction," he says, "but a comparable effort has not been expended to understand how the environment causes impaired human health." Environmental contributions to disease, he adds, are entirely preventable.

At Montreal's McGill University, Abby Littman, a well-known critic of the genome project, worries also about the limitations of the project to solve environmental health problems. "Everything that's been done so far is about managing the genome project," she says, "instead of questioning the whole issue of whether there should be a human genome project."

Littman, a professor in McGill's Department of Epidemiology and Biostatistics, chairs the Human Genetics Committee of the Cambridge, Massachusetts-based Council for Responsible Genetics, a nonprofit genetics consciousness-raising group that publishes *Gene Watch* newsletter.

"Why are we so busy mapping the genome? Why don't we map the environment instead of mapping the genome," she adds, "and worry about things that really make us sick that we don't know anything about? Why do we think it's so much easier to change genes than environmental conditions that put us at risk? Because it's more expensive to clean up the environment than to deal with people who are at medical risk because of the environment."

Littman contends that most human disabilities happen after birth and are caused by accidents, injuries, and other environmental factors that in the long term might be harder to control than genetic disorders. And she believes the public deserves to be educated and have a say in such matters. In terms of genetic technology, "decisions are being made and things are happening that need public airing," she says.

Although Littman agrees that genetic therapy could help create a society where no one is physically or mentally defective, she urges scientists and the public to question genetic goals. Says Littman, "Do we want to live in a society where nobody is born with Down's syndrome? If so, why? That's an ultimate aim of these tests. Does this make us a better society? I'd like to make geneticists think about these questions as they do their work."

Therapeutic Genetics

H.J.J. Leenen, professor of social medicine and health law at the University of Amsterdam, draws another kind of line in the sands of genetic controversy. In his article, "Genetic Manipulation with Human Beings," published in *Biomedical Ethics,* Leenen distinguishes between therapeutic and nontherapeutic genetic engineering. He endorses therapeutic manipulation for somatic cell and germline therapies, but rejects the use of nontherapeutic genetic engineering, which he calls dangerous and unfair to future generations.

"There is a solid ethical and legal basis for therapeutic measures," Leenen writes, "and even for assumptions about the wishes of a future generation. The elimination of suffering and disease justifies decision-making on its behalf." But the situation is different, he believes, for eugenics (hereditary improvement by genetic control) or genetic enhancement. "The present generation should avoid using genetic engineering to impose its own ideas about personality, intelligence, character traits, talents and the like on future generations," he adds.

Prenatal Diagnosis and Reproductive Choice

In his article, "Prenatal Diagnosis and the Ethics of Uncertainty," in *Biomedical Ethics,* Eric T. Juengst describes the moral uncertainty of prenatal diagnosis as a medical practice because prenatal diagnosis is associated with selective abortion.

Juengst, acting chief of the ELSI Program Branch at the National Center for Human Genome Research, concludes that prenatal diagnosis is a tool parents should be able to use to make their own reproductive choices. But, he believes, access to such technology should be denied parents who seek prenatal diagnosis only for purposes of gender identification.

"The moral framework that will guide the practice of prenatal diagnosis as a mature medical technology is still emerging," Juengst writes. "Its foundations are in the ethical traditions of clinical medicine and genetic counseling, with their complementary imperatives to enhance fetal welfare and facilitate parental choice." Juengst continues, "As the next generation of diagnostic techniques raises new moral, conceptual and social uncertainties, the relationship between the traditions will be increasingly important to the practice's moral stability."

There Ought to Be a Law

In terms of NIH's ELSI program, Juengst is fielding criticism aimed at the branch's failure to produce a federal genetic privacy law and at the branch's unsuitability to act as its own watchdog.

"Given what we know about the history of other attempts to develop and introduce sweeping social legislation, . . ." Juengst says, "it's not surprising that three years into the effort we don't have a federal genetic privacy law."

Such an effort, he adds, is roughly equal in complexity to the human genome project itself. The criticism is less about a specific law than it is about "the sense that ELSI ought to deliver some tangible products," he says. "And the most visible kind of product is a law. There ought to be a law."

Asked when it would be reasonable to expect such a law, Juengst says he doesn't know if anyone "could predict the course of a piece of legislation like that." In the meantime, NIH's ELSI branch has delivered several policy-type products (as listed in the progress report) and has others in the works.

On the watchdog issue, taken up in an Office of Technology Assessment background paper released October 13, *Biomedical Ethics in U.S. Public Policy*—Juengst says, "We don't feel the work we sponsor is compromised by fact that we sponsor it. Grantees are free to speak their minds about the issues. On the other hand," he adds, "it is a challenge to corral these academics into a policy-making forum. It's not what NIH is set up to do."

Juengst said the OTA report, which concluded that the United States should have a federal bioethics body, is perceived in the scientific policy and ethics community as a first step in that effort. Juengst said he "would breathe a sigh of relief" at the formation of such a federal commission. For the commission, as well as the public, the challenge will be to manage the work that comes out of the NIH genome project."

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